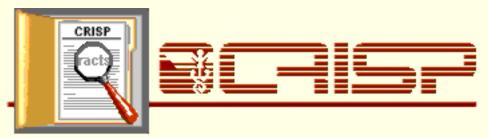
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## **Abstract**

**Grant Number:** 1K01NR007654-01

**PI Name:** ROBBINS, WENDIE A.

PI Title:

**Project Title:** Multifactorial Genetic Disease Model:Schizophrenial/HLA

**Abstract:** DESCRIPTION: (provided by applicant) Schizophrenia is a complex, severe psychiatric disorder that affects up to 1 percent of the world population. Both a strong genetic component and evidence for environmental influences have been demonstrated, yet, specific alleles and/or specific environmental factors have not been identified. An association between schizophrenia and immune responsivity has been suggested, as well as prenatal factors including infection. As with other Psychiatric disorders, clinical heterogeneity, epistatic genetic effects, and multifocal brain involvement have made the etiology difficult to study. Therefore, we propose to use a refined phenotype of severe disease (childhood onset) to maximize discrimination among genotypes and compare alleles in probands versus alleles in non-affected nuclear family members on immune HLA genotype and selected non-immune candidate genes. Data will be used to explore/refine statistical methods that integrate and maximize information for gene-gene interaction testing. The specific aims of the research are to: 1. Genotype immune HLA-A, HLA-B, HLA-DRB1, HLA-DQB1, and non-immune candidate schizophrenia loci Iq32.2-q41, 4q31, 9q2l, and Xpl1.4-11.3 and 2. identify gene-gene interactions underlying the clinical manifestation of childhood onset schizophrenia through the study of the candidate immune and non-immune genes listed above. The training portion of this application is designed to provide solid theoretical foundation, laboratory skill, and statistical knowledge to prepare the candidate for a research career in the area of gene-gene and gene-environment interactions involved in the etiology of complex genetic disorders. The candidate's previous work has looked in a very linear way at induced chromosomal aberrations related to environmental exposures. Such studies are important but limited. The candidate lacks the training necessary for research at the gene or gene and gene/environment

interaction level. Schizophrenia (as an example of a complex genetic disorder) will provide an excellent model for training.

## Thesaurus Terms:

gene interaction, genetic disorder, genetic mapping, genetic model, histocompatibility antigen, immunogenetics, schizophrenia family genetics, gene environment interaction, genotype human subject, patient oriented research

**Institution:** UNIVERSITY OF CALIFORNIA LOS ANGELES

405 HILGARD AVE

LOS ANGELES, CA 90024

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